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Committee Secretary
Senate Foreign Affairs, Defence and Trade Commission
PO Box 6100
Parliament House
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Submission for the Senate Inquiry into the Australian Defence Force Use of Mefloquine and Tafenoquine

The Australasian College of Tropical Medicine (ACTM) is a medical association, whose members include distinguished medical clinicians, research scientists and veterinarians working in the field of tropical medicine in the Australasian region, where it is the pre-eminent professional organization in this field.

We consider that in any enquiry the welfare of patients/subjects is of paramount importance. Some members of the panel have worked with the ADF previously but in this submission, the views expressed are those solely in relation to the scientific evidence at hand.

We intend to confine our remarks to dot point 6 in the Terms of Reference, i.e. international evidence on the impact of anti-malaria drugs of the quinolone class.

MEFLOQUINE

- * Is used by over 35 million people in the last 34 years as a preventive drug. *Ref: Lin Chen, Mary Wilson JAMA 2007 297(26) 2251-2263*
- * is a potent and effective prophylactic agent against all malarial species, including the recently identified *Plasmodium knowlesi*
- * Professor Nicholas (Nick) White, the eminent Oxford University malariologist recently commented "mefloquine is highly effective against *P. falciparum* (the most serious form of malaria) in most parts of the world except parts of SE Asia'
- * is taken once weekly as against doxycycline and atovaquone-proguanil (Malarone or Promozio) that require daily administration. This is important as compliance with the latter drugs is often sub-optimal

Side Effects *Ref: Croft AM Cochrane data-base review showed overall side effects with mefloquine were not greater than with other anti-malarial drugs.*

- * Side effect profile is well known but only 5% have to stop the drug due to symptoms induced.
- * Central Nervous System symptoms include dizziness and nightmares,
- * Contra-indicated in patients with history of psychiatric disorders including anxiety and depression

- * may lower threshold for seizures though a recent study found acute psychosis or major seizures in only 1:10,000 patients.
 - * contra-indicated in patients taking drugs to control cardiac conduction
- teratogenicity - a study of 2,000 pregnant women found no evidence of fetal abnormality; however Nosten (1999) *Ref: F Nosten, Vincenti M, Simpson J. The effects of Mefloquine treatment in Pregnancy. Clin Infect Dis 1999 28:808-811* suggested there may be increased still-births in women taking mefloquine compared to quinine.

TAFENOQUINE

- * has been the subject of clinical trials to find an effective alternative drug if others are no longer effective.
- * historically, a related drug (primaquine) has been taken as a 14 days course to prevent relapse (or recurrence) of *P. vivax* malaria
- * has the advantage of a long half life so allowing less frequent dosage and thus better compliance
- * human and animal trials show it is more potent and less toxic than primaquine and provides protection for up to 10 weeks

Side Effects

Gastro-intestinal disorders are common but mild. In one study, participants reported nausea (31%), headache (29%), dizziness (19%). Like primaquine, tafenoquine can cause breakdown of red blood cells (haemolysis) in subjects with an hereditary enzyme deficiency of red blood cells (G6PD deficiency). A blood test identifies this deficiency. Vortex keratopathy was present in 90% of cases but was not associated with visual impairment and was fully resolved in 12 months. *Ref: Nasveld P, Edstein M et al. Randomised double-blind study of the safety, tolerability and efficacy of Tafenoquine versus Primaquine. Trans R S Trop Med 202. 96 (6) 683-684*

GENERAL COMMENTS

- * The Australian Defence Force (ADF) has been at the forefront of malaria research since WW2 and the Army Malaria Institute is of world standing.
- * These trials took place in 2007-2008 and should be judged on the information available at that time
- * There is no reason to suspect that Australian Army Medical Ethics Committee had not applied a vigorous assessment process before approving these trials, however we recommend that the Committee obtain an independent review of the process employed by the ADF if there is any doubt.
- * In any study, the risks of malaria must be taken into account and the benefits of treatment weighed against the potential side effects of the drugs employed.
- * ACTM would be pleased to provide information pertaining to the scientific aspect of these trials as we have a panel of experts available.

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